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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/614,324

07/08/2003

Norikazu Ueyama

OKA-0209

7360

23353 7590 12/28/2007
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EXAMINER

KOSAR, ANDREW D

ART UNIT

PAPER NUMBER

1654

MAIL DATE

DELIVERY MODE

12/28/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/614,324

Applicant(s)

UEYAMA ET AL.

Examiner

Andrew D. Kosar

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14-19 and 21-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14-19 and 21-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 9, 2007 has been entered.

Response to Amendments/Arguments

Applicant's amendments and arguments filed October 9, 2007 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed below is herein withdrawn.

With regards to the rejection under 35 USC § 103(a), the examiner withdrawn the rejection in favor of new grounds of rejection set forth below.

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

Claims 17-19 are objected to for the following informalities:

Claims 17 and 19 use the variable 'm', however it should be a subscript.

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Claims 17-19 use parenthetical expressions to describe elements, e.g. - (where R₂ represents...), which is not in conformance with current US practice. The parenthesis should be removed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. “Using” is not an active step and thus the claims recite no active step and one cannot practice the invention without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-19 and 22-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 16 and 24 each recite, “where the covalent bond of the functional group of the metal complex with the amino group of the N-terminal amino acid or the protein or peptide (A) or with the carboxyl group of the C-terminal amino acid residue of protein or peptide is formed,” however claims 17 and 19 allow only for bonding to the N-terminal or C-terminal, respectively, and thus the claims lack clear antecedent basis.

Claims 17-19 recite, "is represented by the following general formula," however it is unclear as what is the specific formula if the formula presented is general. It is unclear if this is a general formula whether the metal, M, can have additional ligands, e.g. X type ligands, which are not shown in the 'general formula'. In order to obviate this rejection, applicant is suggested to delete the term 'general'.

Claims 17 and 19 recite the general formula $(L_2)_mM(L_1 \text{ or } 3)$ and that "m is a number of L_2 , indicating 0, 1, 2, 3, 4 or 5," however it is unclear, particularly in view of the described species of claim 18, whether m is describing the additional coordinations to the metal center or whether it is describing the number of discrete ligands. For example, is Applicant describing terpyridine as $L_2 = 3$ where each pyridine unit is considered a discrete L_2 , or is the terpyridine considered $L_2 = 1$?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

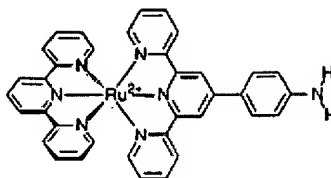
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by
STORRIER (G.D. Storrier and S.B. Colbran. Inorg. Chim. Acta (1999) 284, pages 76-84).

The instant claims are drawn generally to metal complexes of the formula $(L_3)M(L_2)_m$, where L_3 comprises a phenylamine group.

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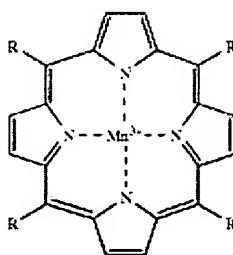


Storrier teaches the complex: . Because the 'reagent' requires no additional elements, nothing precludes the use of the complex of Storrier as the reagent.

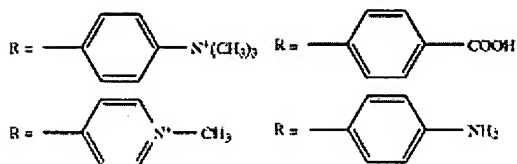
Please note, the amendments to the claim reciting the intended use "for determining..." and the clause, "wherein the covalent bond to be formed..." do not render the claims unobvious or unanticipated, as the structure is taught in the art.

Claims 14, 17, 19 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by CRAPO (US Patent 5,994,339).

The instant claims are drawn generally to metal complexes of the formula (L₃)M(L₂)_m, where L₃ comprises a phenylamine group or the complex (L₁)M(L₂)_m, where L₁ comprises a benzoic acid.

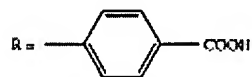


Crapo teaches the complex: , where R is any one of



(e.g. claim 5). Because there are so few choices for R, one could envisage each and every combination, and thus the species where R is

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are anticipated. As above, because the 'reagent' requires no additional

elements, nothing precludes the use of the complex of Storrier as the reagent.

Please note, the amendments to the claim reciting the intended use "for determining..." and the clause, "wherein the covalent bond to be formed..." do not render the claims unobvious or unanticipated, as the structure is taught in the art.

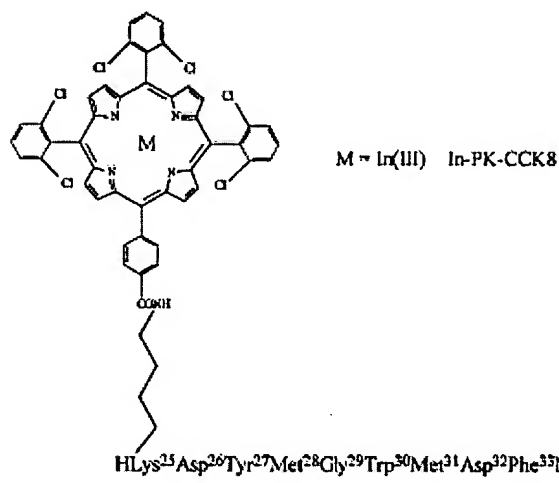
Claims 19 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by LONSDALE (US Patent 4,948,506).

The instant claims are presented *supra*. Lonstdale teaches tetra-(aminophenyl)-porphyrin iron(II) (e.g. claim 6). As above, because the 'reagent' requires no additional elements, nothing precludes the use of the complex of Storrier as the reagent.

Please note, the amendments to the claim reciting the intended use "for determining..." and the clause, "wherein the covalent bond to be formed..." do not render the claims unobvious or unanticipated, as the structure is taught in the art.

Claims 14-17 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by DE LUCA (S. De Luca et al. J. Peptide Sci. (2001) 7, pages 386-394).

De Luca teaches formation of In-PKCCK8,



to the carboxylic acid of the indium(III) porphyrin (page 386). The compound was analyzed by mass spectroscopy (Page 386, "Mass spectra obtained..."), thus meeting the limitations of the claims- forming a conjugate and analyzing the peptide/complex conjugate by mass spectroscopy.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14-17, 19 and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over DE LUCA, *supra*, in view of TAMIKA (H. Tamiaka et al. Bull. Chem. Soc. Jpn. (1993) 66(10), 3062-3068) and CRAPO, *supra*.

The instant claims are additionally drawn to the method where the peptide complex/conjugate is formed with a metal complex with a phenylamine group. Please note, the instant method claim 24 does not *per se* require the coupling to be through the phenylamine group to a carboxylic acid (*see 112 2nd rejection above*).

The teachings of Crapo and De Luca are presented *supra*. Tamiaka teaches conjugation of porphyrins to a peptide through the amine of a phenylamine group (e.g. Scheme 1, page 3063) and analysis of the product by mass spectroscopy (e.g. compound 5Z, page 3068- “*MS m/z 1152*”). Crapo teaches a myriad of peptides can be formed. Furthermore, substituted tetraphenyl porphyrins with a myriad of substitutions on the phenyl moiety are well known by the artisan skilled in the porphyrin arts, as evidenced by Crapo. Additionally, De Luca teaches metallation of the porphyrin prior to conjugation with the peptide.

The difference between the instant claims and the teachings of Tamiaki is that while Tamiaki teaches conjugation of the peptide to the porphyrin through the porphyrin phenylamine group and the analysis by mass spectroscopy, Tamiaki does not teach using the metallated porphyrin in the synthesis.

Selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results (see, e.g., *Ex parte Rubin*, 128 USPQ 440, 1959, and *In re Burhans*,

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154 F.2d 690, 69 USPQ 330 - CCPA 1946) MPEP § 2144.04. Here, the only difference is the step at which the metallation occurs. Thus, it would have been obvious to have metallated the complex prior to the peptide conjugation in the absence of new or unexpected results.

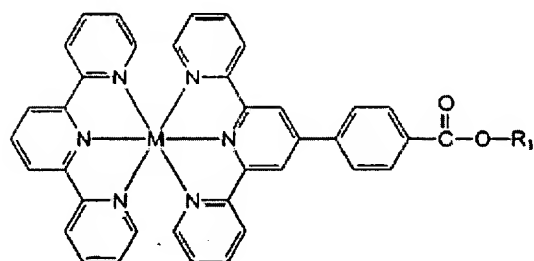
Alternatively, it would have been obvious to have used any of the porphyrins of Crapo in the method of forming a peptide conjugate to the porphyrin, as both De Luca and Tamiaki teach conjugation through both the carboxylates and amines of the peptide with equal success in doing so. Crapo teaches porphyrins which bear both carboxylates and amines which are capable of conjugating and are closely related to the porphyrins of De Luca and Tamiaki. The reference are relied upon for the reasons discussed above. If not expressly taught, based upon the overall beneficial teaching provided by the references with respect to peptide conjugation to porphyrins in the manner disclosed therein, the selection of the conjugating group for connecting the peptide and the porphyrin is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

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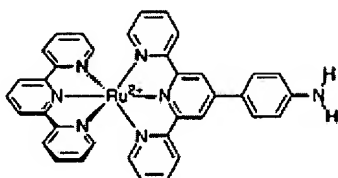
Claims 14, 17-19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over STORRIES, *supra*, in view of SHIRAI (EP 0677293 A1), BARIGELLETTI (F. Barigelletti et al. Chem. Commun. (1998) pages 2333-2334) and/or SAUVAGE (J.-P. Sauvage et al. Chem. Rev. (1994) 94, pages 993-1019).

The claims are drawn generally to the complex



, where R is H.

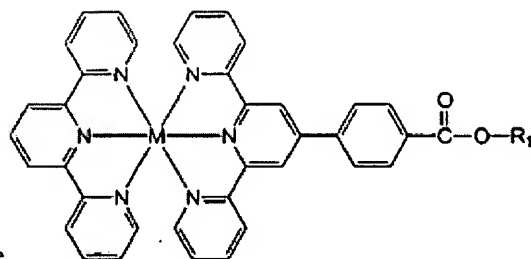
The teachings of Storries is presented *supra*. Terpyridine ligands conjugated to metals is well known in the art, e.g. Sauvage, Barigelletti and Storries. Shirai teaches a variety of 6' substituted terpyridine ligands.



Storries teaches

and teaches the benzoic acid terpyridine as

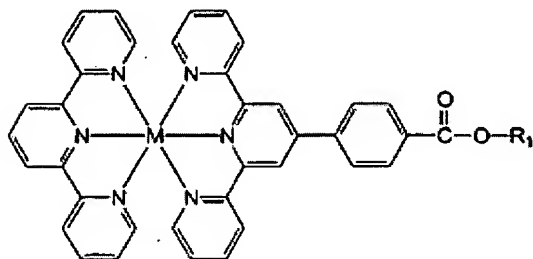
well as conjugation of the benzoic acid terpyridine to a metal core, however Storries does not



teach the discrete conjugate

, where R is H.

It would have been obvious at the time of the invention to have formed the complex



, as the two ligands are all well known to the artisan and coordination of the two ligands to metal cores is also well known to the artisan. Further, coordination of mixed terpyridine ligands is widely practiced in the coordination chemistry arts, and thus would have been obvious to make the compounds with the expectation that they would function as other members of the metal bis(terpyridine) family.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

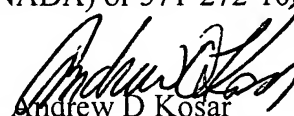
Conclusion

References cited on the enclosed PTO-892 and not relied upon in any rejection are considered pertinent to the instant disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Andrew D Kosar
Patent Examiner
Art Unit 1654